

Applicant : Chen-Kun James Shen  
Serial No. : 09/977,432  
Filed : October 15, 2001  
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Attorney's Docket No.: 08919-016003 / 13A-870916  
(CON)

### REMARKS

This document is filed in reply to the final Office Action dated August 9, 2004. Claims 33-63 are pending. Reconsideration of this application is requested in view of the following remarks:

The Examiner maintained the rejections of all of the pending claims under 35 U.S.C. § 103(a) as being obvious on two grounds. Applicant traverses both grounds, respectively, below:

#### I

The Examiner maintained the rejection of claims 33-36, 41-46, 51-53, and 58-59 over Zhang et al., J. Biol. Chem. 270(15): 8501-8505 ("Zhang") in view of Miller et al., Biotechniques 7(9): 980-990, 1989 ("Miller"). See the final Office Action, the paragraph bridging pages 2 and 3. Applicant disagrees and discusses independent claim 33 first.

Claim 33 covers a viral expression vector that contains, among others, an enhancer having SEQ ID NO:1 or its complement. It is the Examiner's position that this claim is obvious over Zhang (which teaches a non-viral expression vector that has a SEQ ID NO:1-containing HS40 enhancer) in view of Miller (which teaches retroviral vectors containing promoters). According to the Examiner, it would have been obvious to one skilled in the art to include in the Miller vectors the HS40 enhancer taught in Zhang. See the final Office Action, as well as the previous final Office Action mailed December 23, 2003.

In the response dated March 22, 2004 to the previous final Office Action, Applicant pointed out that an enhancer, such as the Zhang vector, which functions in a non-viral vector, may not function in a viral vector; and as a result, one skilled in the art would not have been motivated to make a viral vector containing an enhancer in the manner suggested by the Examiner. To support this point, Applicant submitted a copy of McCune with the response. McCune teaches that (1) an enhancer functions well in a non-viral vector, but fails in a viral vector; and (2) viral vector sequences are responsible for the failure.

The Examiner countered, in the pending final Office Action, that "[Applicant's argument] is found NOT persuasive because the response element as taught by McCune is not

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limited to the responsible element as claimed[,] i.e., SEQ ID NO:1, therefore there is reasonable expectation of success that a response element other than as taught by McCune would function in any viral (retroviral) vector as claimed." See page 6, lines 6-9; emphasis original. It appears to be the Examiner's position that McCune's teaching is only limited to those elements described therein, but not any other elements, such as SEQ ID NO: 1. Applicant disagrees. To the contrary, McCune specifically teaches that "[its] finding may be applicable to the more general problem of sustaining expression of retrovirus-transduced genes..." (See page 4477, column 2, lines 12-13.) Thus, the Examiner has clearly failed to establish a prima facie case of obviousness.

Even if a prima facie case of obviousness were made (which Applicant does not concede), it can be successfully rebutted by a showing of an expected result. More specifically, a SEQ ID NO: 1-containing enhancer "confers position-independent and copy-number-dependent expression on a transgene" (see the specification, page 1, lines 12-19). "This was an unexpected result because, previously, transgene expression was limited by position-effect variegation, silencing of transgenes, and the inability to increase expression by increasing the copy number of the specification transgene." See the specification, page 5, lines 1-5. In contrast, Zhang and Miller, alone or combined, do not teach or suggest this unexpected result. Applicant therefore submits that the unexpected result has successfully rebutted the prima facie case of obviousness allegedly established by the Examiner.

For the reasons set forth above, claim 33 is non-obvious over Zhang, Miller, and McCune. Claim 51 covers a method of using the expression vector of claim 33 and is therefore also not rendered obvious by these references for the same reasons. Neither are claims 34-36, 41-46, 52-53 and 58-59, all of which depend from claim 33 or claim 51 directly or indirectly.

## II

The Examiner also maintained the rejection of claims 37-40, 47-50, 54-57, and 60-63 as being obvious over Zhang in view of Miller and Jarman et al., Mol. Cell. Bio. 11(9): 4679-4689 ("Jarman"). See the instant final Office Action, page 4, lines 15-20. Applicant disagrees. Independent claims 33 and 51, from which all of the rejected claims depend, are discussed first.

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As pointed out in Part I above and in the response to the previous final Office Action, Zhang and Miller do not suggest (1) a viral vector including an enhancer containing SEQ ID NO: 1 or its complement, or (2) this particular enhancer's unexpected property. Jarman teaches a regulatory element of the human  $\alpha$  globin gene. Indeed, it does not teach or suggest making a viral vector containing a regulatory element, such as an enhancer, let alone its properties. In other words, Jarman does not rectify the two deficiencies of Zhang and Miller.

Thus, for the same reasons set forth in Part I above, these three references, alone or combined, would have not suggested the viral vector of claim 33, a vector including a SEQ ID NO:1-containing enhancer. As claim 33 is not rendered obvious by the cited articles, neither is claim 51, which covers a method of using the vector of claim 33. By the same token, claims 37-40, 47-50, 54-57, and 60-63, all of which depend from claim 33 or 51, are also non-obvious over the cited references.


#### CONCLUSION

Applicant submits that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges to deposit account 06-1050, referencing the Attorney's Docket No. 08919-016003.

Respectfully submitted,

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